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With Compliments of the Author.

The Pathology and Morbid Anatomy of Tubercle.

REPORT TO THE

WISCONSIN STATE MEDICAL SOCIETY,

BY

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THE PATHOLOGY AND MORBID ANATOMY OF TUBERCLE.

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As Chairman of your Committee on Pathology, I have endeavored to select a subject for your consideration on this occasion, that should not only be of interest to us all, but should also serve the purpose of eliciting a general discussion, which might lead to practical results. With no little hesitation and misgivings as to my ability to bring the matter before you in a proper shape, I have concluded to call your attention, as briefly as possible, to a very interesting and important topic in pathology, the common property of the physician and the surgeon, viz: The Pathology and Morbid Anatomy of Tubercle. For many years, as the result of microscopical examinations of specimens and chemical observations, I have been firmly convinced that the so-called scrofulous affections of bone, joints and lymphatic glands are tubercular in structure and behavior, and constitute only a link in the chain of development of tuberculosis, as generally understood. When these organs are primarily involved, as is usually the case, it is an indication that the process has not become general, and that by early and well directed treatment, its extension to more important and vital organs might be prevented. In this sense the affection, although not entirely ignored by American teachers and authors, has not received the careful attention its importance and gravity demands. The identity of the disease, as it affects bone and lymphatic glands, no one denies, but the relation it bears to tuberculosis has been a source of warm and often bitter disputes among pathologists. The prevailing ideas concerning this point may be arranged under three heads:

1st. It is a disease *per se*, entirely distinct from tuberculosis.

2d. It furnishes the soil or material for tuberculosis.

3d. It is identical with tuberculosis.

To prove the correctness of the last assertion, which is the principal aim of this report, we must be able to show that it is identical with well recognized forms of tuberculosis, histologically, ætiologically, and clinically. In considering tubercle, as applied to bone and lymphatic glands, it is necessary to utilize the prolific literature on general

tuberculosis which has accumulated since the epoch-creating labors of the distinguished Lænnec. There is, perhaps, no other disease in our nosology about the nature of which there have been entertained more diverse, and often diametrically opposed, views among observers, than the question regarding the true nature and significance of tubercle. Anatomical research and bedside observation have proved alike unsatisfactory in furnishing the desired knowledge, and it is only during the last few years that light is beginning to dawn by way of experiments, which have pointed out to us the correct method of investigation, and have already yielded practical results, the importance of which it is impossible to over estimate. For a long time it was supposed that the lungs were the principal, if not the only primary seat of tuberculosis, hence the term was, and by some is still, applied almost exclusively to indicate the existence of tubercular phthisis. Post-mortem examination and inoculation experiments on animals have shown, however, that almost every organ and tissue in the body may become the seat of the disease, and in fact, that in most cases of pulmonary tuberculosis earlier evidences of the same disease can be found in the lungs or some other part of the body.

The meduallary tissue of bone and lymphatic glands are closely related anatomically, physiologically and pathologically, and are consequently prone to the same affections. It is generally conceded that the so-called scrofulous affections of these organs exert a potent influence in the causation of tuberculosis, but it is my purpose to argue in favor of the identity of the former with the latter. As tubercle of bone and lymphatic glands originates in the same way, and undergoes the same changes as when it affects other organs, it will become necessary for us to study the general subject of tuberculosis, in order to apply the knowledge thus obtained to a better understanding of the disease when it involves these particular organs.

THE RELATION OF TUBERCLE TO INFLAMMATION.

The post-mortem room and clinical observation have taught us that the presence of tubercle, wherever found, is invariably associated with more or less inflammation, but the relationship of the one to the other has given rise to various theories. The same discrepancy of opinion has existed as to the identity or non-identity of the gray, or crude, and the yellow, or cheesy tubercle. Bayle gave an accurate account of miliary tubercle in different organs, but, in addition, described another affection, under the name of miliary granulations, as translucent cartilaginous nodules. He also committed the error to ascribe to the cheesy products of other affections tuberculous properties. Lænnec regarded the miliary granulations of Bayle as a variety of miliary tubercle, and published his well-known views concerning

the transformation of the miliary tubercle into the tubercular infiltration. He accepted Bayle's theory that every cheesy mass is the result of a previous deposit of tubercle, and that every pulmonary phthisis owes its origin to tubercle. Louis advanced the same opinion. Broussais and Andral regarded tuberculosis as a consequence of an antecedent inflammation. Andral was acquainted with the fact that in some instances pus is converted into cheesy matter, and he regarded miliary tuberculosis as a product of a pre-existing pneumonia. Bouchardat attributed to pneumonia no direct influence in the causation of tuberculosis, but considered the general debility following it as a predisposing element, acting in a similar manner as debilitating causes from any other source. Colberg, on examining one hundred phthisical lungs, found that in ninety cases the destruction of tissue was due to cheesy pneumonia, and only ten were affected with miliary tuberculosis; of these, six were complicated with cheesy pneumonia, and in all of them other organs had also become affected. Slavjanski examined 139 lungs from phthisical patients, and found that 123 belonged to the pneumonic, and only sixteen to the tubercular variety. Buhl was the first to call attention to the relation existing between cheesy inflammation and miliary tubercles, the latter of which he considers to be infectious, the result of absorption of a specific virus from the products of foci of caseous inflammation. Virchow regards cheesy inflammation, scrofula and tubercle as distinct and independent pathological conditions, but admits that it is difficult to maintain this distinction by established facts. He taught that the tubercular metamorphosis is not limited to tuberculosis, in its accepted sense, but that it also occurs in new inflammatory deposits and in heterologous formations. On this account he suggested the term cheesy metamorphosis, in place of tubercular metamorphosis.

Lebert looks upon tubercle as a product of inflammation, the rapidity of its development depending on the degree of mal-nutrition of the tissues and the amount of absorption of pathological products.

Reinhardt observed that the tissue changes in organs affected with tubercle, and undergo the same alterations as when they are the seat of chronic inflammation. The distinctive feature of the tubercular process does not consist in the formation of a specific pathological product, but that under its influence the affected organ becomes subjected to repeated attacks of inflammation, usually of a chronic type.

Klebs adheres to the opinion that there must be a specific difference in the products of cheesy inflammation from the beginning, inasmuch as not all cheesy material is capable of generating miliary tuberculosis, and that this difference in the virus does not depend on anatomical conditions, as the formation of capsules, etc. He recognizes an intimate causative relation existing between scrofula and tuberculosis. To support this view, he mentions the anatomical condition of lymphatic glands in the immediate vicinity of miliary

deposits. In cases of cheesy degeneration of bronchial glands he has witnessed a corresponding portion of the lung infiltrated with miliary tubercle, while no trace of tubercle could be found in any other part of the body.

Niemeyer, as well as Virchow, affirms that the infiltrating tubercle of Laennec is the product of inflammation, consequent upon an attack of chronic pneumonia, particularly the catarrhal variety. Pidoux regards cheesy pneumonia and tuberculosis as manifestations of one and the same diathesis.

The observations of Aufrecht on tubercle of the peritoneum have induced him to speak of the process as a peri-lymphangitis.

Max Schüller speaks of the tuberculous process as being of an inflammatory nature. Inflammation does not consist of simple migration of white and diapedesis of red blood corpuscles, but a change is always found to exist in the pre-existing histological elements, as has been sufficiently proven by the researches of Virchow, Stricker and Ranvier; this cell abnormality, of course, Schüller attributes to the presence of micrococci. While caseous degeneration is a general characteristic of tuberculosis, it is, in his opinion, a later and secondary change, for the parts which have undergone metamorphosis, are the same as have been the seat of a specific tubercular inflammation, and are, at the same time, matrix and product of this inflammation. Inflammation necessarily precedes caseation. It is true that caseation often follows closely on the heels of tubercular inflammation, but in other cases it does not take place for a long time, and occasionally it does not make its appearance at all. Schüller does not accept the theory of insufficient nutrition as the cause of caseation, but attributes this change to the action of the tubercular virus, which, at an earlier period, excited the tubercular inflammation.

M. Litten reports three cases of sero-fibrinous pleuritis, which were followed by acute miliary tuberculosis. In two of the cases there appeared to exist a hereditary taint to tuberculosis. The development of tubercle followed closely the resorption of the effusion. In most cases of acute miliary tuberculosis there can be found in some organ a cheesy deposit, or the products of an antecedent tubercular deposit. Litten argues further, that although auto-infection by means of products of simple inflammation is known to take place, it does not necessarily follow that the infecting material possesses specific qualities, as the absorption of regressive products of inflammation will produce, in some cases, similar results. Acute affections, as typhoid fever, and especially measles, may be the cause of tuberculosis in individuals predisposed to this disease. Any irritation, if continued for a sufficient length of time, may become the cause of tuberculosis. Inflammation follows the application of irritants, and when the products of this inflammation necrose the absorption of the detritus, may be followed by tuberculosis. Tubercular nodules ex-

cite inflammation in the organs in which they are deposited, hence tubercle may be either the cause or effect of inflammation. C. Ruge and Waldenburg have asserted that irritation alone may produce tuberculosis, entirely independent of any caseation.

Birch-Hirschfeld commits himself on this subject as follows: "The development of the neoplasm called tubercle is connected with inflammation of a definite type."

The existence of tubercular eruptions in the vicinity of caseous deposits, gave rise to the opinion that the cheesy material elaborates a virus which produces a specific neoplasm—the tubercle.

Ziegler, in commenting on the results of his experiments with inert substances in producing tuberculosis in animals, advances the following propositions: "Tubercle, with its giant cells, is a focus of inflammation, in which the colorless blood corpuscles accumulating at any point undergo a peculiar development. Tubercle might be regarded as a degenerated species of inflammatory neoplasm (granulation), determined by necrobiotic processes.

David Foulis makes use of the following plain language in expressing his views on this subject: "Tubercle is the result of a local inflammation, set up in certain cells of low vitality, by irritation either from solid particles or from fluids of a composition unsuited to them."

Billroth, in studying the development of tubercle in the mesentery, was impressed with the fact that the initial lesion usually takes place at a point where small blood vessels take a sudden turn, an anatomical arrangement which diminishes the rapidity and force of the blood current. In the tubercular process the endothelium and white blood corpuscles participate. The number of cases where miliary tuberculosis exists without cheesy deposits is growing constantly less, as post-mortem examinations are more carefully made. Tuberculosis is not hereditary, but the pre-disposition to chronic inflammation is inherited. Every person who has a cheesy deposit is liable to suffer from tuberculosis at any time.

Treves remarks: "Tubercle is no neoplasm, but the product of a peculiar form of inflammation."

Wilson Fox claims that there exists a close relationship between tuberculosis and cheesy pneumonia.

Morbid anatomy furnishes abundant proof that in most cases of diffuse miliary tuberculosis evidences may be found of previously existing local tuberculosis in the form of caseous deposits, and where these cannot be found they may have disappeared before the time of examination, or been overlooked during the examination. In the light of recent experiments it must be admitted that tubercle, as such, is never the product of simple inflammation; inflammation, however, may so alter the properties of the tissues as to furnish a favorable soil for the development of tubercle. It is also a well known fact

that the presence of tubercle will, unless it has become latent, excite inflammation of a chronic character, which is modified in its tendencies by the tubercular process. The origin and growth of tubercle is attended by cell proliferation within, and in the immediate vicinity of capillary vessels resembling ordinary inflammation; but the course of the process and the future fate of the exudation material is modified by the tubercular virus imparting to the tubercle nodule specific qualities found in no other product of inflammation or neoplasm. Only cheesy material, the result of an antecedent tubercular deposit, can give rise to diffuse miliary tuberculosis. All other inflammatory products can only serve as a fertile soil for the localization of tubercle, thus furnishing only one of the conditions for tuberculosis. Inflammation around the tubercle nodule favors local progression, but is only one of the consequences of local infection.

INOCULATION TUBERCULOSIS.

Inoculations with tubercular matter were made at an early day, to prove the infectiousness of the disease. The first experiments of this kind were made by Kortum in 1789, and Cruveilhier in 1826. In 1834 Erdt succeeded in producing numerous nodules in the lungs of horses by inoculating them with scrofulous pus, and Klencke, in 1843, produced tuberculosis of the lungs in rabbits, by injecting tubercular matter in the jugular vein. These experiments attracted but little attention until, in 1865, Villemin announced the results of his investigations in this direction. He succeeded in communicating tuberculosis from man to animal by means of inoculation. His experiments consisted in the subcutaneous introduction, behind the ears of rabbits, of fragments of tubercle or fluid from the cavity of a tuberculous lung recently removed from a patient who had died of pulmonary tuberculosis. The first animal was killed three one-half months after inoculation; the lungs and most of the internal organs were found diffusely infiltrated with miliary tubercle. His numerous experiments yielded similar results, and led him to the following conclusions: "Phthisis of the lungs (like tubercular diseases in general) is a specific affection. Its ætiology depends on an inoculable agent. It can be readily communicated from man to animal by inoculation.

Tuberculosis, therefore, belongs to the class of virulent diseases, and deserves, nosologically, a place side by side with syphilis, but is perhaps more closely related to glanders."

Inoculations with pus from phlegmonous abscesses, discharges from cholera patients, and anthrax tissue, produced negative results.

Vogel repeated the experiments of Villemin on horses, without success.

Biffi, Verga and Sangalli experimented on mules, cows, sheep, dogs, cats, mice and chickens, with negative results. The experiments of Langhans led him to the conclusion that tubercle could not be communicated in the manner described by Villemin, the inoculation material only acting as a foreign body, the inflammation following its introduction differing in no way from the ordinary forms of inflammation.

Among those who made successful experiments and adopted the doctrine advanced by Villemin may be mentioned: Hèvard and Cornil, Hoffman, Cohn, Béhier, Empis, Mantegazza, Bizzozero, Lebert and Wyss, Klebs, Koester, Waldenburg, Bijuen, Simon, Sanderson, W. Fox, Papillon, Nicol and Laveran. Hèvard and Cornil were able to propagate tubercle when they inoculated with genuine tubercular matter, but failed with cheesy material. Marcet inoculated eleven guinea pigs with the sputa of tuberculous patients, and in ten of them the experiment proved successful. Lebert and Wyss made numerous experiments with various substances, as pus, cancer and sarcoma tissue, coal-dust, mercury, etc., and finally concluded that, although when using the products of tubercular inflammation, disseminated pneumonia, infiltrated glands, and granulation tissue, multiple infectious nodules are most readily produced, the same result may be obtained with products of inflammation and heterogeneous substances, only not so readily and constantly. Waldenburg's inoculation experiments with different substances led him to the belief that all substances used must enter the circulation, and while there act the part of a foreign body, producing capillary embolism, the small thrombus serving as a nucleus for the miliary nodule, around which the white blood globules extravasate and are converted into tubercle corpuscles.

Klebs is a firm advocate of the specific virulent nature of the tubercle as taught by Villemin. The following are his views: "Tuberculosis can be transmitted from man to animals by inoculation. By inoculation with tuberculous matter a form of affection of the lymphatic glands can be produced which resembles perfectly the scofulous lymphatic affections in man. Inflammatory processes accompanying the inoculation of tubercle in animals takes place only in case the inoculating material has undergone putrefaction, or when it has been contaminated with mechanically irritating substances, or when the inoculation wound has been exposed to external irritating influences. The detritus of non-tuberculous tissue, as well as fine granular inorganic substances, if introduced into the body, can, under certain conditions, produce microscopical changes resembling tubercle, which, however, differ materially from tubercle anatomically, as well as in their future behavior."

R. Volkmann declares that tubercle in man readily inoculates *in loco*, but in contradistinction to experimental inoculations in ani-

mals, it is slow in becoming general; rapid diffusion can only take place under peculiarly favorable circumstances. Cohnheim is willing to acknowedge that as yet we are not able to give a correct anatomical definition of tubercle or tuberculosis. Tubercle is not a definite anatomical entity. He believes that tubercle is the product of a specific virus, and that tuberculosis can only be produced by tubercular matter. Animals infected with tubercle present the particular symptoms of tuberculosis in man, and none other. Like Virchow, he rejects the doctrine that caseation is the criterion of tuberculosis, as advocated by Laennec. He attributes to tubercle as high a degree of infectiousness as to the virus of vaccination or syphilis. In man infection usually takes place through the respiratory passages, and the disease is very apt to manifest itself primarily at the point of infection. He furnished a beautiful illustration of the last assertion, by injecting tubercular matter into the anterior chamber of the eyes of rabbits, which invariably produced tuberculosis of the iris. C. Hueter also succeeded in producing tuberculosis of the iris by introducing into the anterior chamber of the eye small fragments of granulation tissue, taken from a joint affected with fungous synovitis. M. Hippolyte Martin, in considering the identity or non-identity of true tubercle and the so-called pseudo-tubercle, produced by inoculation with inert substances, maintains that by the results of a series of inoculations a criterion is furnished which distinguishes one from the other. Inoculations with true tubercle were followed by diffuse miliary tuberculosis in the inoculated animals, and inoculations can be successively made without diminishing the intensity of the disease. Inoculations with pseudo tubercle never give rise to general tuberculosis, and the infectivity of the product is lost at the second or third series of inoculation.

M. Toussaint, in a communication to the Academie de Sciences de Paris, asserted that true tubercle, both in man and animals, reproduces itself indefinitely with absolutely constant and identical properties, and that it is capable of being transmitted from animal to animal without losing its virulence; in fact, its virulence increases with the number of re-inoculations. The first inoculation requires from four to five months to kill a pig or rabbit, while material taken from the fifth series of inoculations requires only two months to produce a fatal termination of the disease. Products of the cultivation of tubercular virus manifest the greatest virulence. The pseudo-tuberculosis produced by inoculation of inert substances may resemble true tuberculosis in many respects, but it is incapable of being reproduced in the same manner.

Some interesting experiments have been performed by M. M. Krishaber and Dieulafoy on the artificial production of tubercle in monkeys. The conclusions drawn from these investigations are: 1, That human tubercle, when inoculated, kills a monkey in nine out of

ten cases, with lesions analagous to those met with in man. 2. The effect of the inoculation varies according to the substance employed; the gray granulation is most, and the pulmonary parenchyma least infectious. 3. Two monkeys only were found to be insusceptible.

Dr. V. Lentz has recently made experiments with blood from tuberculous rabbits. The fresh blood from a tuberculous rabbit, he injected into the trachea of six rabbits. The animals were killed in from 92 to 216 days, and two of them were found affected with tuberculosis. Blood from one of these was injected into the knee-joint of another rabbit, which resulted, after eighteen days, in caseous degeneration of the joint and pulmonary tuberculosis.

Max Schneller's experiments with blood from tubercular animals yielded similar results, and strongly tend to prove that the infectiousness of tubercle does not depend on the presence of caseous material, but on a virus which is capable of being diffused through the medium of the circulating fluids of the body.

Lippl, Schweninger and Tappeiner claimed to have produced tuberculosis in rabbits, with inhalations of atomized sputa from tubercular patients, while Schottelius says he produced the same result with a single insufflation of an indifferent substance. Ziegler believes that the result was not tuberculosis, but miliary foci of inflammation. Finely divided substances, inhaled into the lungs, enter the bronchial tubes and alveoli, and migrate into the interstitial substance of the lungs, the lymphatic vessels, and finally are arrested in the lymphatic glands. In any of these localities these foreign bodies may excite irritation, and form a nucleus for an inflammatory nodule.

These inhalation experiments have been lately repeated by Weichselbaum, of Vienna, dogs alone being employed. Eleven experiments were made with tuberculous sputum. The duration of the experiments varied between two days and two and one-half months, and the number of inhalations between one and twenty-four. In all these cases, even in those in which only one inhalation had been administered and the animal killed one or two days afterwards, tubercles were found in the lungs and kidneys, many nodules in the former, one or two only in the latter. Moreover, the bronchial glands, and in some the mesenteric glands also, were swollen, and presented tubercles under the microscope. Inhalations of emulsions of cheese and bullock's spleen, yielded negative results. Pus from a carious rib, diluted with water and inhaled for seven weeks, produced only a few nodules in the lungs, although these had a structure similar to the tubercles of the first series. The same subject has been investigated in France, by M. Giboux, and in an aspect of more direct practical importance. The nocuity or innocuity of the air expired by phthisical patients, was the point examined. He collected daily forty or fifty litres of air expired by persons in the second or third stage of phthisis, and passed half this air into a hutch in which were two young rabbits, born of perfectly

healthy parents. Two other similar rabbits were confined in another cage of similar construction, and through this was passed daily twenty or twenty-five litres of the remaining air, which had been filtered by being passed through tow, impregnated with carbolic acid. The two cages were placed in separate rooms, so as to prevent any contamination of the air of the one by the respiratory products from the other. The experiment lasted from January 15th to April 29th. At the end of this time, the two rabbits placed in the second cage were in perfect health, while the others suffered from loss of appetite, thirst, diarrhœa and emaciation. At the autopsy, tubercles were found in the principal viscera, and the lesions in the lungs were much more advanced than in the other organs. On the other hand, the viscera of the two rabbits in the second cage, presented no trace of tubercle.

Tuberculosis has also been produced in animals by feeding them on tuberculous matter. Successful experiments of this kind were made by Chaveau, Aufrecht and Bollinger. Bollinger found that herbivorous animals acquired the disease in this manner more readily than the carnivorous, and that the omnivorous, and among them probably man, resembled more the first class of animals in this respect. Among the animals infected by feeding tubercle, the following were the most important changes found at the autopsy: Intestinal ulcerations, tuberculosis of the mesenteric and portal glands, and in several instances also of the glands of the neck.

Colin's experiments were unsuccessful. The experiments of Klebs, in propagating tuberculosis by feeding animals with food containing tuberculous matter, would tend to show that localization of the disease primarily takes place at the point of infection,—the intestinal canal, and that it becomes general through the medium of the portal circulation.

Ziegler is of the opinion that inoculations and inhalations of substances not possessing specific properties, have excited products closely resembling tubercle, and which cannot be distinguished from it anatomically. He argues, however, that not the production of tubercle, but the clinical history of inoculation tuberculosis, is the most important element. Progressive infection is the most characteristic feature of tubercle. Miliary tuberculosis is an infectious disease, the course of which can often be traced step by step. The lymph vessels are the channels through which the infectious material is conveyed into the blood. In how far infection can take place through the lungs, is not well ascertained. When caseation takes place in the interior of an organ, infection has taken place through the medium of the blood. He is also inclined to believe that germs destroy the vitality of the cells in the nodule, acting, at the same time, as irritants to the neighboring tissues.

Fehleisen claims that not all of the products of a tubercular inflammation are carriers of a specific virus, but the virus is diffused through

the medium of cheesy matter, cheesy pus, in fact, the products of degeneration. This view is supported, from a clinical stand-point, by Volkman, who says: "Wherever the tissues of the healthy body come in contact with softened cheesy material and pus, containing the tuberculous virus, and wherever this pus is conveyed, there arise eruptions of specific miliary formations, and numerous miliary eruptions mark the way where the specific products have taken their course. These eruptions yield again new infectious and inoculation material, as soon as they have become degenerated into cheesy material." Fehleisen inoculated the peritoneal cavity of rabbits with granulation tissue, from a case of fungous arthritis, also with small pieces of the lining membrane of a cold abscess, taking the precaution to avoid the introduction of cheesy material. The peritoneal cavity was selected on account of its well-known property of affording the most favorable surface for rapid absorption. Twenty experiments were made. Two of the animals died, one on the forty-first, the other on the sixty-fourth day after the operation. A post-mortem examination revealed that in both animals the peritoneum and pleura costalis and pulmonalis were thickly studded with miliary tubercles, and scattered nodules were found in most of the organs. The remaining animals, eighteen in number, were killed from the fiftieth to the ninetieth day after the inoculation, and all of them were found to be perfectly healthy, and no trace of tubercle could be found in the peritoneum or any other organs. These facts induced the experimenter to conclude that in the two fatal cases infection was probably produced by cheesy pus, which may have been adherent to or contained within the inoculating tissue.

J. Orth belongs to the class of pathologists who believe that animals can be successfully inoculated with tubercle, and that the artificial product is identical with tubercle as found in man.

Baumgarten, in opening a discussion on tuberculosis, in the Medical Society of Koenigsberg, made the assertion that not all cheesy deposits are capable of giving rise to tuberculosis. To prove this statement, he said that animals prone to cheesy inflammation rarely suffer from spontaneous tuberculosis, and that in man, cheesy deposits in cutaneous and syphilitic growths seldom provoke the disease. According to his views, only tubercular caseous deposits can infect the organism with tubercular eruptions.

During a discussion on Inoculation Tuberculosis, in the Berlin Medical Society, Friedländer asserted that although an affection resembling tuberculosis has been artificially produced in animals, by the introduction of tuberculous or cheesy matter, or even inert substances, the clinical behavior was at variance with the genuine disease. He injected from twenty to forty C. C. of an emulsion of cheesy material, taken from a human cadaver, into the small veins of the neck of a dog. Of twelve animals inoculated in this manner, only one

died, and in this case from an accidental disease. The remaining eleven dogs were killed in from three to four weeks after the operation. In ten of the animals, nodules the size of a pin-head were found in the liver and spleen, less constantly in the lungs and kidneys, and never in the pleura, eye or pia mater, and only in one instance in the peritoneum. The animals never suffered from local or constitutional symptoms. In the lungs, the nodules consisted of alveoli, filled with epithelial cells. The microscopical appearances corresponded closely with the lobular desquamative pneumonia of Buhl. The giant cells, which are almost constantly found in tubercle of man, were never found. In reply, Waldenburg stated that Friedländer's description of the artificial disease in animals corresponded with the affection as found in man, with the exception of the absence of giant cells, and, according to Virchow, these cells do not constitute a specific element of tubercle. Waldenburg, Klebs and Hering have found the giant cells in the nodules of inoculation tuberculosis, and Friedländer was ready to admit that they were not uniformly present in tubercle of man. Waldenburg has observed the same clinical history in the infected animals, as in tuberculosis of man. The diffusion of tubercle depends on the place and manner of inoculation.

Friedreich regards the anatomico-pathological stand-point as insufficient to explain the nature of tuberculosis. Clinical observation and ætiological influences must be added to arrive at correct conclusions. He has found giant cells in typhoid products and in leukæmic nodules.

Zenker considers experimental pathology of great importance in ascertaining the nature of disease. He was surprised at the results of his experiments on animals, which were made in accordance with the method practiced by Villemin. He is satisfied that tubercle is transmissible from man to the lower animals by inoculation. Inoculation can be practiced successfully by introducing the tuberculous material under the skin, into the peritoneal cavity, the veins, anterior chamber of the eye, or any other place that can furnish an absorbing surface. The period of incubation varies from two to four weeks.

GERM THEORY OF TUBERCULOSIS.

The results obtained by the simple inoculation of gray tubercle or cheesy material, have been so widely at variance, that experimenters were divided into believers and non-believers in the infectiousness of tuberculosis. The large class of pathologists, who maintained the theory of its infectiousness, were therefore anxious to isolate the virus giving rise to infection. These efforts resulted in the germ theory of tuberculosis, which has recently attracted so much attention among physicians and scientists. Moretto had already suspected that scrofu-

lous diseases depended on the presence of low organisms, and C. Hueter ascribed to them an essential part in the genesis of scrofula. The first experiments with isolated cultivation germs, were made by Klebs, in 1877. He found, by examining fresh specimens of tubercle of human lungs, that they invariably contained a species of bacteria, small granules, about one-thousandth part of a millemetre in diameter, and twice as long, possessing spontaneous motion. Transferring these germs through a series of cultivation fluids, composed of albumen of eggs or Bergmann's cultivation fluid, he found that they retained their vitality and infectious properties. The third cultivation product proved to be pure and reliable. Injections of these germ-containing cultivation fluids were made under the skin, into muscles, lungs, pleural and peritoneal cavities, and if the animals survived the operation for any length of time, they soon became tubercular. Injections of cultivation fluids, containing the germs of tissue from scrofulous glands and lupus tissue, were also promptly followed by tuberculosis.

Max Schueller repeated the experiments of Klebs with the same results. He described the specific germs as round and rod-like bacteria, the rods presenting bulbous extremities, which are not infrequently bent to one side, and are composed of two, seldom more, spherical bodies. They are found most numerously in the tissues of diseased joints, where large colonies may be seen in the synovial membranes of contused joints in animals which had been infected with tubercle a few days previously. They are first noticed in the extravasated blood in contused joints; the blood appears to serve the purpose of a cultivation fluid. They become more distinct on the application of ether and a solution of caustic potassa; a blue color is imparted to them by methyl violet. From the infected joints the micrococci enter the juice canals of cartilage, which become dilated. When they reach the bone, they infiltrate the cancelli; large colonies can be seen on the margins of osteomyelitic deposits. In the small blood and lymphatic vessels the micrococci adhere to the tunica intima; their presence excites irritation, which manifests itself by an increase in the size of the preexisting cells, rapid reproduction of tissue elements, migration of blood corpuscles, stasis, coagulation of blood and lymph, and finally complete obstruction of the vessels. Transverse sections of such vessels present the appearance of giant cells. Micrococci affect the white corpuscles more than the red. The former under their influence appear larger, and adhere to each other, forming masses, thus contributing largely to the rapid occlusion of minute vessels. The infected district furnishes a favorable soil for reproduction of the germs, hence the process of infection is progressive, and continues indefinitely. Casation is the result of the deleterious effect of the micrococci upon the newly formed tissues. The infection may remain local for an indefinite period, provided the local conditions are un-

favorable for diffusion or multiplication of germs, or when these are rendered innocuous or are exerted.

In a discussion on tuberculosis, at a meeting of the Vienna Medical Society, Billroth said that the theory of the parasitic nature of tuberculosis is not to be cast aside, because the investigation of the parasitic element is a matter of great difficulty, while acknowledging that in regard to the heredity of tuberculosis in the same sense as the heredity of syphilis, nothing is known, he believes that the parasitic hypothesis must suppose a special predisposition to tuberculosis in certain individuals, and he agrees with Niemeyer's well-known view that the scrofulous diathesis predisposes to tuberculosis. Neoplasms become more rapidly disseminated, when the local and general condition is one of debility. We also know how rapidly the organism will eliminate certain kinds of parasitic germs, as hyphomycites; when, however, the conditions of life of these germs are changed by cultivation in alkaline fluids kept at the temperature of the body, then their introduction into the body is followed by the most disastrous results, a fact which has been most conclusively demonstrated by the experiments of Grawitz. The germs under these conditions multiply with such great rapidity, that all efforts on the part of the white blood globules to eliminate them are futile, and they literally inundate and overpower the organism.

In speaking of the parasitic origin of tuberculosis, Ziegler asserts that not all cheesy deposits give rise to infection, but that their infectious property depends on the presence of specific micro-organisms, the caseous material only furnishing a favorable soil for their development. Naegeli has called these germs Schistomycites, and Ziegler adopts this term. Naegeli has ascertained that these germs are rendered innocuous by the acid secretions of the stomach, but that they again become active when in contact with the alkaline fluids of the intestinal canal, hence the stomach is never, the intestinal tract on the other hand frequently, the seat of tubercular ulceration. The germs are miasmatic in the air, but acquire contagious qualities in the organism. The virulent germs from phthisical patients may be conveyed directly to other persons, or through the medium of the air or soil. Ziegler is so firmly convinced of the parastic origin of tuberculosis, that he adopts the phrase, "No phthisis without noxae," as one of the closing arguments of his excellent paper.

Perhaps no subject in medicine ever excited more universal and intense interest, than the recent announcement by Robert Koch of his discovery of the specific germ of tuberculosis, the *bacillus tuberculosis*. Not long ago, Cohnheim, an enthusiastic advocate of the infection theory of tuberculosis, made the assertion that "the direct demonstration of the tubercular virus must to this day be considered an unsolved problem." Experimental pathology and improved methods of microscopical examination, have at last enabled Koch to isolate, cul-

tivate and demonstrate a germ, which he has found invariably present in all recent tubercular products, and which he considers to be the specific agent in the production of the disease. By his process of staining the objects for examination, the bacilli appear of a delicate blue, and the organic tissues of a brown color. The bacteria are rod-shaped, and belong to the family of bacilli. They are very narrow, and in length about one-fourth to one-half the diameter of a red blood corpuscle. They resemble the bacilli of lepra, but are more slender and pointed at each extremity. These bacilli are present in clusters in great numbers in fresh tubercular deposits, and they may often be seen in the interior of cells. On the border of cheesy foci they are usually found isolated; when softening takes place, they disappear. When giant cells are present, they always contain bacilli, even if they are not found anywhere else. From the fact that they are found present in these cells without exception, it must be assumed that they are active in their production, as they disappear as soon as degeneration takes place. In 11 cases of acute miliary tuberculosis, Koch found the bacilli in all of them. In 12 cases of caseous bronchitis and pneumonia, he found them along the border of cheesy deposits, and very numerous in cavities. From other kinds of bacilli, they may be distinguished by their blue color on staining, while other forms of bacilli are stained brown by the same process. He found them also present in one case of primary tuberculosis of brain, the deposits having assumed the size of a hazel-nut, also in two cases of intestinal tuberculosis, in two cases out of three of extirpated scrofulous glands, and in two cases out of four of fungous synovitis. They were found constantly in cases of spontaneous and inoculation tuberculosis of animals. Inoculation tuberculosis was observed in 172 guinea pigs, 32 rabbits and 5 cats, and in all of them the bacillus was found. That the bacillus is the cause of the tuberculous process is evident from the fact that the germ is always found in places where the process is most active, and always disappears as soon as retrograde metamorphosis has taken place.

In order to prove that these germs were the essential cause of the disease, he isolated them from the tissues, and submitted them to a series of fractional cultivation. As a cultivation material he took serum from the blood of an ox or sheep, which was solidified and sterilized by exposing it to a temperature of 58°—65° C. for a sufficient length of time. Under strict antiseptic precautions tubercle tissue from lung, or caseous lymphatic glands from recently deceased animals, was conveyed to test tubes containing the sterile soil, and kept at the temperature of the body, great care being exercised to prevent the ingress of any additional atmospheric germs. After ten days colonies of bacilli were seen on the surface of the soil, and as they do not possess spontaneous motion, they did not penetrate into its interior. Some of these germs were carefully removed to another

test tube, when the same process repeated itself; thus it was possible to generate the germs through a series of cultivation, without losing their virulence or capacity for reproduction. Under antiseptic precautions, guinea pigs were inoculated in the groin with the products of the cultivation. The day after the operation the wound was usually found healed: on the eighth day a nodule appeared at the point of operation, which usually ulcerated. After two weeks, swelling of inguinal and sometimes of axillary glands appeared, followed by rapid emaciation, and death after the expiration of the fourth to the sixth week. At the autopsy tubercles were found in almost all of the organs, but most numerous in the spleen and liver.

Inoculation of the anterior chamber of the eye produced promptly local tuberculosis, followed by general infection. Injections into the peritoneal cavity and veins of the ear, were followed by the same consequences. The microscopical examination of products of inoculation tuberculosis presented the same histological elements as the spontaneous form. These facts go to show, that the bacilli are not accidental companions of the tubercular process, but that they are the essential *cause, noxae or agens* of the disease. Not the presence or peculiar arrangement of cells, not the non-vascularity of the product, but the presence of bacilli, is the diagnostic feature of the disease. The majority of cases of scrofulous affections of bone and lymphatic glands, reveal the presence of bacilli, and are consequently identical with tuberculosis. If tuberculosis is a parasitic disease, we must endeavor to show where the germs came from. The germs develop only when kept in a temperature of from 30°—41° C., hence their vital or active existence is limited to the animal organism. In man tubercle is found most frequently in the bronchial tubes and the lungs, from inhalation of air contaminated with the bacillus. All conditions which favor the developement of the germs are in direct ætiological relation to the disease. Although Dr. Koch was not the first to conceive the brilliant idea of isolating the tubercular virus from the crude products of tubercle, and cultivating the same artificially outside of the body, he has nevertheless immortalized himself by his zeal in investigating the ætiology of tuberculosis, and in improving the methods of investigation. Using solid or semi-solid substances as a "*Nährboden*," contamination is avoided with greater accuracy, and the process of germ development can be watched with greater ease. The results of his experiments are so striking, that the most incredulous must soon be convinced that we are on the verge of the greatest discovery in medicine—the isolation and artificial production of the tuberculosis virus.

Telluric influences undoubtedly either favor or retard the development of the specific germs of tuberculosis, as it is well known that the arctic regions offer a certain degree of immunity against tuberculosis, while the tropical countries furnish the greatest number and the most acute cases. An altitude of 2000 feet above the level of the

sea, may be considered the boundary line for the frequent occurrence of tuberculosis; a dry, sandy soil and a dry atmosphere are also unfavorable for the growth of the germs, and clinical experience has sufficiently demonstrated that these conditions exert a favorable influence towards the prevention, arrest and cure of tuberculosis.

In a communication to the Medical Society of Berlin, Dr. Ehrlich describes a new method for detecting the bacilli of tubercle in the sputa of tubercular patients, which, on account of its excellence, is destined to supercede that of Koch. He extracts, with a pair of needles, a small particle of sputum, and presses it between two cover-glasses. He then separates the cover-glasses and has a thin layer of sputum on each. The cover-glasses are allowed to dry in the air, and in order to fix the albumen, they are either kept for an hour at a temperature of 100 C.-110 C., or they are passed two or three times through the flame of a Bunsen's burner. The staining fluid is then prepared. Water is shaken up with an excess of aniline oil, and filtered through moistened filter-paper. To the clear fluid so obtained, an alcoholic solution of methyl-violet, or of fuchsin is added, drop by drop, until the fluid becomes opalescent. The cover-glasses, with the dried sputum, are then set swimming in this fluid, and in fifteen or thirty minutes they will be stained an intense blue or red, according as the violet or fuchsin has been used. Dr. Ehrlich now departs further from Koch's method; he does not color the substance in general with vesuvin, but decolorizes it with strong acids, the bacilli retaining the blue color. One volume of officinal nitric acid is mixed with two of water, and the blue-stained preparations are placed in this strong acid. In the course of a few seconds the color fades, a yellowish cloud passes across the preparation and leaves it white. Everything in the preparation of the sputum is now decolorized, except the bacilli, which are intensely blue. But the technical difficulties of seeing them are still considerable, and it is further desirable to color the ground substance yellow, in the case of a methyl-violet, and blue in case of a fuchsin preparation. In the specimen of phthisical sputum prepared by Dr. Ehrlich, as above, and exhibited at a meeting of the Royal Medical and Chirurgical Society of London, the bacilli were very numerous, very uniform in size and form, and very distinct, the magnifying powers about 900 diameters, and the illumination strong. Dr. Ehrlich has examined the sputa from twenty-six pronounced cases of phthisis, and he has found bacilli in all of them, and most abundantly in acute cases.

Baumgarten gives the following method of staining tubercle bacilli, as easier and more expeditious than those recommended by Koch and Ehrlich: Dry preparations of tubercular sputa are made according to Koch's or Ehrlich's method, and moistened with a very dilute solution of potash. The bacteria can then, without further treatment, be readily detected with a power of 400-500 diam. Light

pressure on the cover-slip will serve to bring them out more clearly. In order to distinguish the bacilli of tubercle from other species, the cover-slip is removed from the slide and laid to one side, until the moisture on its under surface has dried off; it is then passed two or three times through the gas flame, and moistened with a drop of dilute aniline violet, or other nuclei-staining aniline color. Now under the microscope, the putrefactive bacteria are stained a deep blue, while the tubercle bacilli remain perfectly colorless, as when in the potash solution. The entire process need only require ten minutes, and is therefore recommended for general use.

It now seems certain that the inoculation experiments of Villemin and his followers, and more recently the inoculation of isolated germs, obtained from cultivation fluids, have at last succeeded in establishing, beyond all doubt, the infective nature of tuberculosis on a scientific basis. Experimental pathology has been the means of unraveling the mysteries of one of the most frequent and destructive of all diseases, and is now inviting the therapeutist to pursue a similar course to discover a rational and effective course of treatment. It is to be hoped that these investigations will be continued until we shall be perfectly familiar with the mode of introduction, the conditions of life and the diffusion of these germs, and then the time will not be distant when we shall be able not only to arrest, but also to prevent the ravages of this, the most frequent and hopeless of all diseases—tuberculosis.

HISTOLOGY OF TUBERCLE.

The anatomico-pathological basis of tubercle was created by Virchow, and has been firmly established through the laborious researches of Langhans, Wagner, Klebs, Schueppel, Rindfleisch, Koester, Friedländer, Fox, and many others. The specific cell theory has had many able advocates, and has been the topic of many animated discussions, but it has at last been abandoned as fallacious and unscientific. There are no specific tubercle or scrofula cells. When we speak of tubercle, we mean a nodule or granule, which is composed of certain histological elements. The anatomical character of the nodule consists, not in the presence of any one particular element, but in the peculiar arrangement of the cells, and this is the only reliable anatomical guide in making a diagnosis.

Virchow defines tubercle as a nodule representing a heterogeneous growth, a production originally necessarily of a cellular nature, taking its starting point from the connective tissue, or from some analagous tissue, as marrow, fat, bone. These nodules (miliary) when mature are often so small that they cannot be recognized with the naked eye, but usually they are as large as a millet seed, or even larger. When the nodules become confluent, they may form masses the size

of a walnut, surrounded by a common zone of embryonal tissue. The primary nodules are quite firm and of a gray translucent color. Virchow has subdivided the miliary into submiliary granules, each of which contain the essential element of tubercle, and by aggregation, constitute the ordinary miliary nodule. The yellow tubercle is a more advanced stage of the gray, the histological elements of the latter having undergone caseation.

Colberg has shown that tubercles in the lungs originate from the nuclei of the capillary vessels, the connective tissue and alveolar cells never being primarily affected. The transition from miliary to yellow tubercle, he attributes to a blocking up of the interior of the capillary vessels by the new product, and a consequent arrest of the circulation, thus diminishing the supply of nutritive material.

Edward Smith believes in the epithelial origin of tubercle.

Bastian observed tubercle nodules upon the small vessels in cases of basilar meningitis, but refers their origin not to the nuclei of the endothelial lining of the vessels, but to the endothelial lining of the perivascular lymphatic sheaths through which the vessels of the meninges of the brain take their course. Virchow credited the endothelial cells in the lymphatic vessels with taking an active part in the production of tubercle before Bastian published the result of his observations, but was unable to convince himself of the fact.

Julius Klebs holds that the endothelial cells of lymphatic vessels are the primary seat of tubercle. He observed that in cases of tubercular ulceration of the bowels, the peritoneum is reached through the lymphatic vessels, the latter containing tubercle corpuscles in their interior. Silver stained preparations of inoculation tuberculosis from rabbits showed that the finest points of tubercular material were deposited in the interior of the lymphatic vessels at their points of intersection. At some points the nodules extended into the tissues between the lymphatic vessels, but their center always corresponded to the location of a lymphatic vessel. In some places the nodules were seen to send out projections, but the projections in reality were within the lymphatic vessels, as the network of lymphatic endothelium could be seen above and beneath the tubercle corpuscles. Towards the center of the nodule no endothelial cells could be distinguished, and this fact led him to the inference that the normal endothelial cells are directly concerned in the production of tubercle. In the mesentery he saw the tubercles adhere to the outer wall of the capillary vessels, and as the spindle-shaped cells of the outer coat appeared to be pushed apart, he looked upon the adventitia as a genuine lymphoid structure.

Knauff demonstrated the lymphoid character of the adventitia by examining the capillary vessels of the pulmonary pleura of dogs which had been exposed for a long time in an atmosphere impregnated with coal-dust. He found the pigment lodged in small masses close

to the walls of small arteries and veins. Examining the same locality in healthy dogs, he found it occupied by opaque whitish-gray nodules, surrounded by round and oval cells, containing nuclei and a few lymph corpuscles. The same structures, which he called lymph-nodules, are also found around the small vessels of the human pleura, and by an abnormal increase of lymphatic elements they become the primary seat of tubercle.

Manz has studied the development of tubercle in the choroidea in patients suffering from general miliary tuberculosis. So constantly does this disease show itself in this structure that v. Graefe, Cohnheim, Fraenkel and Bouchut recommend ophthalmoscopic examination as a diagnostic measure. Manz traces the origin of the disease in the choroid to a multiplication of the cells of the tunica adventitia of the small vessels. The process is, however, not limited to this structure; the non-pigmented stroma cells may also assist in furnishing material for the new product.

Bush, on the other hand, asserts that the vessels in cases of tuberculosis of the choroid are not primarily affected; the process depends entirely on a degeneration of the stroma cells, as the remaining tissues presented a normal appearance. Cohnheim refers the origin of tubercle in these cases to small, pale, finely granular cells resembling lymph and pus corpuscles—the contractile migrating cells of Recklinghausen, which may be seen between the pigmented and non-pigmented stroma cells.

Rindfleisch traces the beginning of the process in miliary tuberculosis of the lungs to a proliferation of the endothelium and the external connective tissue layer of the capillary lymphatic vessels.

In contra-distinction to the ordinary or lymphoid form of tubercle, there has recently been described the fibrous tubercle, distinguished by its pearl-like, light gray appearance, but possessing the same inherent tendency to caseous, fatty degeneration. It is said to be found most frequently in dense fibrous tissue, and quite often in newly-formed connective tissue. It is composed of nodules of dense connective tissue, the cells of which have undergone rapid growth, containing frequently a number of nuclei. A farther development only takes place in the interior of the nodule, later no trace of round cells is found, the interior undergoing a retrograde metamorphosis into a fatty granular mass, somewhat striped, surrounded by a capsule of connective tissue.

The description of fibrous tubercle by Langhans differs materially from the above. According to his observations, its favorite location is in the so-called parenchymatous organs, as the lungs, liver, spleen, kidneys, testicles, epididymis, and brain. The larger nodules are composed of three zones. The interior consists of a few connective tissue fibres, free oil-globules, and cells infiltrated with fat granules. The middle zone is composed of all the elements of a fibrous groundwork,

the fibres of which are placed in a parallel direction to the tubercle. As the cells of this zone are not numerous, it presents the appearance of a capsule; in reality, however, it is not a capsule for the purpose of constituting a barrier to the further extension of the nodule, but it is the essential matrix of the internal tubercle tissue. He considers this form of tubercle not as a distinct special form, but as a more advanced stage of development of the ordinary variety.

Schueppel is also of the opinion that the fibrous tubercle is only a variety of the common tubercle.

I believe it must be generally conceded that the fibrous tubercle differs from the ordinary cellular variety only in so far that it contains a larger amount of connective tissue, which may be due either to an excess of pre-existing connective tissue in the organ which has become the seat of tuberculosis, or to an active proliferation of the reticulum of the tubercle. Shakespeare and Simes claim that the fibrous tubercle is most frequently met with in sypilitics, and that the granulation or lymphadenoid tubercle occurs most frequently in the scrofulous.

In a clinical lecture on miliary tuberculosis, given before the Vienna Medical Society, Dr. Hans Chiari called attention to another variety of tubercle—the hyaline tubercle. It was first observed by Chiari in the miliary tubercle from the liver of a child aged four years and a half. The tubercles in the brain, lungs and bronchial glands in the same case presented the ordinary aspect of lymphoid tubercle. The clear hyaline aspect of those in the liver gave them a very peculiar appearance. The change is believed to depend on a hyaline degeneration of the reticulum, and resembles most closely the hyaline degeneration of the capillaries of the brain. Dr. Chiari conjectures that it may be regarded as a benign change opposed to the caseation which tends to infection.

Microscopists have made diligent search for a morphological element, which, when found present, should be diagnostic of tubercle.

Lebert's tubercle corpuscle is a thing of the past, and is only referred to, to indicate a landmark in the history of tuberculosis. Reinhart soon showed that these elements, regarded by Lebert as characteristic and diagnostic of tubercle, were present in all products of inflammation, and that their product was only an evidence that a certain amount of inflammation or degeneration of the tubercular nodule had taken place.

A great deal has been said and written, *pro* and *con*, as to the origin and diagnostic value of the giant cell in the tubercular nodule. Langhans discovered it in tubercular tissue, and as he found it uniformly present, he regarded it as an essential anatomical element of the tubercular nodule. In his description of the cell, he placed great stress upon its uniform size and the peripheral location of the nuclei. The giant cell, as described by Friedländer, consists of a mass of protoplasm, containing a number of nuclei. It was first discovered

in normal tissue by Robin, and subsequently accurately described by Virchow. In a normal condition it is constantly found in bone and the placenta. According to Kœlliker, giant cells are found in such parts of bone where resorption is most active during the growth of bone. These cells are also found in fat tissue, especially in cases of rapid emaciation. Kundrat has observed them in inflamed serous membranes, and Stricker and Heitzman in the inflamed cornea. They are usually also found around encysted foreign bodies in the peritoneal cavity and subcutaneous tissue. Langhans found them around blood-clots, after injecting fresh blood under the skin of animals. Friedländer found them present in air cells of the lungs, when in a state of chronic inflammation. For a long time it has been well-known that they are frequently found in the interior of the alveoli of cancer. The protoplasm is composed of a coarsely granular albuminous substance, often containing granules, and the nuclei are usually arranged towards the margin of the cell. In regard to the function of these cells but little is known. They are supposed to be the active agents in processes of absorption, more especially that of bone (Kœlliker). The origin of cells is traced to epithelial cells (Zielonko, Weigert), to endothelial cells (Kundrat, Herrenkohl, Zielonko), or to atrophic growth of nuclei of fat cells, endothelial cells or connective tissue (Virchow, Flemming, Ziegler). Ziegler saw giant cells develop from white blood-corpuscles, while Schueppel and Rindfleisch believe that they invariably originate within blood-vessels or lymphatics, where they constitute the first step towards the development of tubercle nodules. Around this cell the other elements are arranged successively.

Hering, Aufrecht, Woodward, Schueller and Treves hold that these giant cells are not true cells, but that they only represent spaces, corresponding to transverse sections of lymphatic vessels, the protoplasm being the coagulated lymph within these vessels, and the nuclei enlarged swollen endothelial cells. These cells have been studied with such great care in connection with tubercle, by Virchow and Friedländer, and their opinions regarding their cellular structure are so conclusive and positive, that we can hardly fail to be convinced of the correctness of their observations. In tubercle the source of giant cells remains unknown; it is rational, however, to assume that they are developed from preexisting cell elements, or that they are the result of a confluence of several cells. They have been observed to exhibit amœboid movements. They are capable of absorbing smaller elements, as blood-corpuscles and pigment molecules. Their existence does not necessarily indicate the presence of tubercle, as they are found in other pathological products, and form a part of some of the normal tissues of the body. They constitute an almost constant and important element in tubercle, and from their central location in the nodule and the peculiar arrangement of the remaining cellular

elements around them, valuable diagnostic information is obtained. The presence of the giant cell is, therefore, only one of the requirements for a positive diagnosis.

In every tubercle nodule we find the epithelioid cells first described by Rindfleisch and so called from their resemblance to epithelial or endothelial cells. They are about two or three times the size of a white blood corpuscle, finely granular, and contain one large and a number of small nuclei. They may be seen aggregated around the giant cells, occupying the space between them and the peripheral zone of embryonal tissue. They are supposed to originate from white blood corpuscles (Schueppel, Ziegler, Treves), endothelial cells of lymph spaces (Aufrecht, Hering, Woodward), or from the endothelial cells of the blood vessels and lymphatics or connective tissue cells as described by Rindfleisch and nearly every other writer. The remaining cellular element in tubercle is the lymphoid or white blood corpuscle found in great numbers between the giant cells and the epithelioid cells, and forming a complete and compact peripheral zone around these cells.

The reticulum, according to most authors, consists of the pre-existing connective tissue pushed asunder by the cellular elements. According to Wagner, Schueppel, Brodowski, Thaon and Ziegler, it is made up of protoplasm. According to Buhl, the giant cells and epithelioid cells secrete a substance at their periphery which, on becoming hard, is formed into a mass resembling connective tissue; only the marginal zone is supplied with the loose ready formed connective tissue of the organ. According to Wahlberg the principal reticulum consists of protoplasm which is traversed by a network of connective tissue.

A mature typical tubercular nodule consists, then, of a delicate tissue, densely packed with one or a number of giant cells in the center, a large number of epithelioid cells near the center, and lymphoid elements disseminated throughout the nodule and forming a dense marginal zone. The blood vessels and lymphatics in the nodule from intra and inter-vascular cell proliferation become blocked during the early stages of the development of the tubercle, rendering the neoplasm non-vascular, a condition which necessarily leads to early retrograde metamorphosis of the new product. No single element of tubercle can be regarded as characteristic, but a combination of the different elements and their peculiar relations to each other, associated with the non-vascularity of the product, can and must be considered as diagnostic.

LOCAL AND GENERAL INFECTION OF TUBERCLE.

The clinical behavior of tubercle is characteristic and diagnostic. The anatomical peculiarity of each tubercle nodule is such that of

necessity it must speedily undergo caseation; to this rule there is no exception. The circulation in the vessels has become completely arrested by intra and peri-vascular cell proliferation almost from the beginning of the process, thus arresting further supply of nutritive material, and in addition the cell elements composing the nodule are possessed of such a low degree of vitality, that they are incapable of being transformed into living tissue, hence they undergo fatty degeneration. The process of breaking down begins in the interior of the nodule and proceeds towards the periphery. When caseation has taken place, if from any cause the infectiousness of the local deposit has ceased, a favorable termination may take place by a complete or partial absorption of the product, the former being possible only when the nodules are very small, or, what is more frequent, by calcification or cretafication, a result which is frequently observed in the lungs. Softening and suppuration may afford a complete outlet to all tubercular material, as in the case of tuberculosis of the lymphatic glands, and thus lead to a permanent recovery. If the tubercular deposit is located in the skin or any of the mucous membranes, and softening and suppuration take place, it results in the formation of obstinate tubercular ulcerations, or fistulous tracts, which very seldom terminate in complete repair.

In some organs, more especially in the lymphatic glands, the progress of the disease is sometimes arrested by the formation of a firm capsule around the caseous mass; in this manner the infectious material is isolated and prevented from invading the neighboring tissues. These favorable terminations are the exception, the growth of the tubercle, local and general infection, the rule. The growth of the tubercle nodule takes place partly by segmentation of the nuclei of the newly formed elements, but mostly by conversion of the normal cells in the vicinity of the nodule under the influence of a moderately active or passive hyperæmia. By the growth of a number of such nodules, confluence takes place, which results in the formation of masses of considerable size. The local infection takes place through the medium of the cellular elements charged with the infectious germs. The white blood corpuscles possessing, as they do, active amœboid movements, readily insinuate themselves into the surrounding lymph spaces and thus become active carriers of the tubercular virus, establishing new foci of disease wherever they become lodged. The growth of the nodule is progressive; its extent corresponds to the area of the infected district. The tubercular process knows no anatomical boundary line, its onward march is slow but sure, it attacks vessels, connective tissue, glands, membranes, skin, cartilage, bone, etc., alike, and converts or displaces any and all of them.

It has been supposed by many that the presence of a caseous deposit is necessary to give rise to miliary eruptions of tubercle, inasmuch as the gray tubercle is usually found around the margins of

caseous masses. It is, however, more than probable that these caseous foci are the product of a previous tubercular deposit, and that the gray granulations constitute the starting point of the disease, caseation following step by step the onward march of tubercle. When tubercle has resulted in the formation of an abscess, the lining membrane of such abscess is invariably infiltrated with miliary tubercle and the process of infection follows the course of the abscess. This explains why the so-called scrofulous abscesses have always proved so rebellious to the usual methods of treatment, and why so many of these cases have been followed by diffuse miliary tuberculosis.

Tubercle manifests also an inherent tendency to general infection. The local infection is usually a slow process, and may give rise to great destruction of tissue, but is seldom the direct cause of death, unless it interferes with the function of some vital organ, while general infection, on the other hand, usually assumes a rapid course and almost invariably leads to a fatal termination. The manner of infection is the same as in local infection, only that the histological elements which carry the specific germs are conveyed along the lymph or blood current to distant organs, where they establish numerous new foci of the disease. The lymphatic current is usually the medium of communication where the primary depot is located in the skin, in a mucous or serous membrane, or in a lymphatic gland; on the other hand, when the disease is primarily located in a joint or bone, it reaches the internal organs through the blood current leading to metastatic or embolic tuberculosis. I will illustrate this by reporting two cases:

Case I.—*Primary Tuberculosis of Lymphatic Glands of Neck, followed by Miliary Tuberculosis of Lungs.*—Francis Schuhmacher, aged 18 years, was admitted into the Milwaukee Hospital April 6th, 1882. The history of the case does not show any hereditary taint in her family. She has always been a strong, healthy girl until about a year ago, when she noticed a glandular enlargement on the right side of the neck, just beneath the angle of the jaw. Menstruation has been regular, but scanty. The parents of the patient noticed that soon after the glandular enlargement made its appearance she became paler than usual, and complained of lassitude and loss of appetite. The primary swelling was soon followed by a whole chain of enlarged glands, extending from the ear to the clavicle on the affected side. The family physician instituted the usual course of treatment advised in such cases, but without signal success. The patient passed into the hands of another practitioner, who applied poultices to favor suppuration. He punctured two of the largest glands, but no pus escaped. From this time the patient rapidly became worse; redness and tumefaction around the punctures followed. At the time of admission the patient presented an extremely anæmic appearance, but little, if any, emaciation. The

whole right side of the neck from the ear to the clavicle presented one large mass of enlarged glands. At the points of puncture I found two large ulcerations from which protruded masses of cheesy material, the source of an extremely offensive odor. The skin over the cheesy masses was reddened and undermined for a considerable distance from the margins of the ulcerated excavations. The glands which were not ulcerated varied in size from a small orange to that of a hemp seed. It was evident that local infection had spread beyond the reach of the knife, still I was anxious to extirpate the glands which communicated with the air and thus remove a great source of irritation and suffering. The patient was etherized, and, with the assistance of Drs. Naumann and Marston, a mass of lymphatic glands, and among them the ulcerated glands, were removed. The superficial and deep glands were affected. The capsule around the largest glands was very thick and firm, and all the glands presented a greater or less amount of caseous degeneration. The wound healed kindly, and the patient was permitted to leave the hospital a week after the operation.

July 6th, 1882, the patient called at my office. The wound had nearly healed. The remaining glands had not enlarged much since the operation. About four weeks after the operation she began to suffer from a dry, harassing cough, fever and night sweats. Temperature 103°, pulse 140; she had become greatly emaciated, and an examination of the chest revealed the existence of miliary tuberculosis, affecting principally the right lung. At the time of writing (August 3d) I hear that the patient is very feeble and is not expected to live more than a few weeks. This case is of great interest, as it illustrates the progress of the disease step by step along the lymphatic channels until it reached the lungs. It also teaches an important lesson, not to tamper with tubercular lymphatic glands, but to resort at once to radical treatment by early and thorough removal of the local deposits.

Case II.—*Synovitis Hyperplastica Granulosa of Ankle-joint, Evidément. Death from Metastatic or Embolic Tuberculosis.*—L. McKennon, aged twenty-three years, laborer, was admitted into Milwaukee Hospital Dec. 25, 1881. No disposition to scrofula or phthisis present in his family, and he has always enjoyed good health until about a year ago, when, while working in the pineries, he sprained his left ankle. The joint remained painful, but he was able to walk without crutches until two months ago. At the time of admission, he suffered great pain with nocturnal exacerbations. The joint was swollen and a sense of fluctuation could be felt below each of the malleoli; superficial veins enlarged and leg atrophied. The patient was considerably emaciated and his appetite impaired. No signs of pulmonary or renal difficulty could be ascertained at this time. As the patient objected to an amputation, it was decided to

open the ankle-joint and remove the diseased tissues as thoroughly as possible. The operation was performed under strict antiseptic precautions, Feb. 22, 1882, with the assistance of Drs. Naumann, Lang, Mendel, Mueller, Massmann and Martin. The ankle-joint was opened freely on the inner and outer side, when a mass of fungous granulations made its appearance, and a small quantity of sanious flocculent fluid escaped. The articular cartilage was completely destroyed, pieces of considerable size lying loose in the joint. The articular ends of the bones were rough, presenting a honey-comb appearance, and considerably softened. All diseased structures were thoroughly removed with a sharp spoon and gouge. The joint was well drained and immobilized. No inflammation or fever followed the operation. Suppuration was slight, but the wound at no time manifested a tendency to repair. The patient's general condition did not improve, and about four weeks after the operation a slight cough and rise of temperature induced me to examine his chest again. Fine crepitation could be heard all over the chest, and the patient began to fail rapidly and died April 16th, 1882. Two days before his death he complained of intense headache, and soon became delirious.

At the autopsy it was ascertained that the scraped ends of the bones were rough, having shown no tendency to reparative action. The lungs were studded with miliary tubercles throughout, the largest number being found at the base and margin. Smaller and less numerous nodules were found in the liver, spleen, kidneys and meninges at the base of the brain.

In this case we must take it for granted that at the time of operation secondary deposits had already taken place in the lungs, or that the local product in the joint was not completely removed. The practical lesson to be learned from this case is to operate early in similar cases, and to secure a complete removal of the infected tissues either by complete excision or amputation. The arrangement of the vessels in bone is such that infected elements readily enter the blood vessels and then find their way into the pulmonary capillaries and from them into the general circulation. When the infecting agents are carried along the lymph current, they generally are arrested in the nearest lymphatic gland, thus preventing a rapid general invasion. The infected lymphatic gland serves the purpose of a cultivation fluid for the development of the germs, and soon sends along the lymph current new infecting elements, which invade a neighboring gland, and thus the process is repeated until the disease reaches a vital organ, or the germ-laden elements reach the general circulation and initiate an embolic or metastatic tuberculosis.

When the germ-holding elements take a more direct route by entering the general circulation at once, they reach the lungs, where they are usually arrested in the capillaries, giving rise to diffuse miliary tuberculosis of the lungs. Some of the germ carriers may pass

directly through the capillaries, or may issue from one of the new nodules in the lungs, and again enter the circulation and become deposited in a more distant organ, in preference in the spleen, liver, kidneys and brain, thus giving rise to general diffuse miliary tuberculosis. As a rule such organs or parts of the body are most prone to become the seat of infection which offer the greatest amount of mechanical difficulties to the circulation, or where the rapidity of the current has become impeded by some antecedent pathological condition; in other words, stasis predisposes to the localization of tubercle.

HEREDITY OF TUBERCULOSIS.

Almost all text books insist that tuberculosis is an hereditary disease, being, in the majority of cases, transmitted from parent to offspring. So firmly is the profession impressed with the correctness of this assertion, that in every case of suspected tuberculosis, diligent search is made to ascertain who is responsible for the disease. If by chance it is ascertained that one of the relatives of the patient was afflicted with a cough, and died at a premature age, then the diagnosis is considered as settled. It is not difficult to conceive how unreliable in many instances such information may be; but it is difficult to understand in what manner a great-grandfather, an uncle, an aunt or a cousin could transmit the disease, without being able to trace a direct continuation through the parents of the patient. The so-called scrofulous affections have always been recognized as being frequently the cause of tuberculosis; recent anatomical and experimental research, as well as clinical observation, however, tend to establish their identity; hence any facts bearing on the question of the heredity or non-heredity of scrofula will assist in proving or disproving the hereditary nature of tuberculosis.

A weakness of lymphatic vessels in scrofulosis was recognized by Sylvius as early as 1695, by Portal in 1809, and still later by Bell, Percival Pott, Hufeland and Broussais. Fox is of the opinion that a disposition to tuberculosis may be found in certain anatomical or physiological defects in the lymphatic system. Virchow ascribes the cause of scrofula to a weakness or imperfection in the arrangement of the lymphatic apparatus, C. Hueter to a dilation of lymph spaces; and Billroth to a constitutional anomaly.

Byford, in speaking of the exciting causes of scrofula, says: "They are abuses which, in an ordinary condition of the system, would lead to common local inflammation or congestion."

Mordhorst regards a sluggish circulation, the consequence of superficial, imperfect respiration, by causing capillary stasis, and favoring diapedesis, a potent factor in producing the peculiar vulnerability of

the tissues in scrofulous subjects. The capillaries of lymph vessels are composed of a delicate, structureless membrane, lined on the inner side by endothelial cells, and these vessels surround like a sheath the capillary blood vessels and small veins. In scrofula patients, these lymph channels are filled and become blocked with white blood corpuscles, which elements, under certain conditions, are transformed into tubercular structures and invade lymphatic glands. Tuberculosis of the lungs follows when these metamorphosed blood corpuscles reach the subclavian vein and are conveyed into the pulmonary capillaries.

Rokitansky placed great stress on the importance of an imperfect circulatory and respiratory apparatus as a predisposing cause to tuberculosis. By removing venous stasis, the rapidity of the lymph current is increased, and the tendency to glandular swelling diminished.

In 1871 Friedländer suggested that in cases of tuberculosis there might be present, and active, a fusion of the scrofulous and tubercular diathesis, a view which was endorsed by Charcot in 1877.

Aufrecht claims that the disposition to the origin of tubercle may be found in the lymphatic vessels. Riedel defines the hereditary predisposition to tuberculosis, as consisting in a peculiar anatomical arrangement of the tissues, especially of the lymphatic glands, which furnish a favorable soil for infection. According to Max Schüller, the heredity of tuberculosis is greatly overrated. The germs which are supposed to be the specific agents in the production of tubercle, exert a direct effect on the tissues, exciting a slow form of inflammation, with a tendency to speedy retrogade metamorphosis of the new material. Quincke recognizes a close relationship between scrofula and tuberculosis, when he says: "Scrofulous persons are especially predisposed to tuberculosis; tuberculosis hardly ever occurs except in scrofulous persons."

Ziegler was aware that pulmonary phthisis is the most frequent cause of death in scrofulous patients. James T. Whittaker, in comparing the ætiology of tuberculosis with syphilis, makes use of the following positive common-sense language: "There is no such a thing as a predisposition to either disease. Either a man has syphilis or he has it not. One man is not more predisposed to either disease than another. Syphilis affects one individual more than another because its virus finds a better lodgment upon mucous membrane. Tuberculosis finds also, fortuitously, a better nidus in one case than another. The virus of tuberculosis is lodged in one case and not coughed up, just as in syphilis the virus is secreted and not washed off." And again: "From any chancre, plague, gumma, or other deposit of syphilis, reabsorption may take place at any time, and reinfection with syphilis, or better, reappearance of external signs. So, from any caseous nodule, wherein the tuberculous virus is locked up in tempo-

rary innocence, absorption may take place under favoring circumstances, and a new outbreak of tuberculous symptoms appear, the quantity of virus thus set free determining, to a great extent, perhaps, the virulence of the symptoms. While the virus is thus locked up the disease is latent, when set free it is manifest." Wynne Foot says: "Tubercles are small-celled overgrowths of lymphatic tissue (as in acute miliary tubercle) that have preserved such uniformity of size, color and shape, as to have long suggested the probability of their lymphatic origin." Wilson Fox describes tubercle as "an overgrowth, or hyperplasia of lymphatic tissue, resulting from irritation of the lymphatic elements."

W. S. Savory, in speaking of the relation of scrofula to tubercle, remarks as follows: "It appears to me that there is nothing sufficient to warrant the pathological distinction which it is now the fashion to make between scrofula and tubercle." And further: "Tubercle may be said to be the essential element of scrofula." According to Rokitansky, the most frequent seat of tubercle in children is in the lymphatic glands.

Virchow holds that scrofula constitutes the basis of tubercle, and that in man tuberculosis depends in general on scrofula. He says further: "On account of the histological identity of the scrofulous and tubercular new growths, it is often impossible in a given tubercular lesion, to determine how much is inflammatory and how much is tubercular."

From above quotations it becomes apparent that nearly all authors recognize, if not the identity, at least a close relationship between scrofula and tuberculosis, consequently any facts bearing on the heredity of the former, will apply with equal force to the latter. So-called scrofula implies a diminution of the relative amount of blood to the solid tissues (Rindfleisch), and an anatomical and physiological defect in the capillary blood-vessels or the lymphatic system, conditions highly favorable to the occurrence of stasis and a low grade of inflammation. The scrofulous habitus, then, may be looked upon as furnishing one kind of soil favorable for the development of tubercle, and in this sense the hereditary predisposition to tuberculosis must be considered as established. It is only reasonable to assume that congenital defects in the composition of the blood, the blood-vessels, the lymphatic apparatus and the lymph-spaces may occur as frequently and regularly as many other well-known anatomical peculiarities, the heredity of which has long been known and classed among undoubted facts. But this does not establish the heredity of tuberculosis. Hereditary tuberculosis would imply that the specific germs were transmitted from parent to offspring through the medium of the semen or ovum. A person with an inherited disposition to scrofula, will enjoy immunity from any active manifestations of the disease, just so long as he can be kept free from infection with the specific

germs of tuberculosis. Let such a person be exposed and he will be in constant danger of becoming a victim of tuberculosis. After infection has taken place, localization of the tubercle process will occur in that organ which presents the least amount of resistance to infection, on account of congenital or acquired defects.

The reputed hereditary tendency of tuberculosis owes its origin to the fact that children of tubercular parents, born, perhaps, with a defective body, have been exposed, more or less, either directly or indirectly, to infection with specific germs from the sputa of phthisical parents, which may be communicated through the medium of the air, water, food, clothing, etc., and finding a favorable soil, propagate the disease. Place children of tubercular parents under the most favorable hygienic conditions, prevent infection by isolation or a thorough and well-directed system of disinfection, and tuberculosis will become a preventable non-hereditary disease.

I will close by submitting to your further consideration and discussion, the following conclusions :

I. Tuberculosis is an infective, specific, parasitic disease.

II. Scrofula and tuberculosis are identical, pathologically, ætiologically, anatomically and clinically.

III. Tubercle is the product of a chronic, specific type of inflammation.

IV. No single histological element of the tubercle nodule can be considered as diagnostic, but the non-vascularity of the nodule, and the peculiar arrangement of the cells, furnish the necessary requirements for rendering a correct diagnosis on an anatomical basis.

V. The prominent clinical feature of tubercle consists in its tendency to local and general infection.

VI. No organ or pathological product can become the seat of tubercle independently of the action of the specific germs of tuberculosis.

VII. Tuberculosis is not a hereditary disease, but a predisposition to it may be, and then consists in an anatomical defect of the lymphatic apparatus, or the capillary vessels, combined with a diminution in the relative amount of blood to the solid tissues of the body

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